Original Study

ABO BLOOD GROUP DISTRIBUTION IN PATIENTS WITH ORAL SQUAMOUS CELL CARCINOMA

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ABSTRACT

Aim: This study aimed to assess the ABO blood group distribution in patients with oral squamous cell carcinoma (OSCC).

Materials & Method: This descriptive, analytical study evaluated 113 patients complaining of oral lesions presenting to Imam Reza and Sina Hospitals in Tabriz and Dental School of Tabriz University of Medical Sciences from 2011 to 2014, for whom, a definite diagnosis of OSCC was made. The age and sex of patients, location of lesion and family history of cancer were recorded. The blood type of patients was determined according to their blood card or by blood typing. Our control group included 2000 blood donors with no systemic disease. The blood type of control subjects was also recorded.

Results: Of 113 OSCC patients, 70.7% were males and 29.3% were females with a mean age of 67.51±14.29 years. Of all, 24.1% were in the age range of 60 to 70 years. Blood type A was the most common (33.8%) among OSCC patients. The frequency of blood type AB was significantly higher while the frequency of blood type O was significantly lower in OSCC patients compared to controls. Data were analyzed using analytical (chi-square test and t-test) or descriptive (mean and standard deviation) statistics via SPSS version 16.

Conclusion: Presence of A and B antigens on cells may increase the risk of OSCC. In our study, blood type O had a significantly lower and blood type AB had a significantly higher frequency among OSCC patients compared to controls.

Key words: ABO Blood Group System; Blood Group Antigens; Oral Squamous Cell Carcinoma

Introduction

Cancers of the head and neck require utmost attention due to their special anatomical location, their effect on facial appearance, their hidden nature and complex treatment.[1] Squamous cell carcinoma (SCC) is the most common cancer occurring in the head and neck region.[2] SCC is the sixth most common cancer in males and the 15th most common cancer in females.[3] SCC of the head and neck was ranked eighth in terms of cancer mortality worldwide in 2008.[4] The incidence of oral cancer is high in developing countries and it has been reported that two-thirds of new patients are detected in developing countries.[5] Oral cancer is reportedly the most common malignancy after the cervical and stomach cancer in developing countries.[5] The recognized risk factors for SCC include cigarette smoking, tobacco use (chewing/smoking), alcohol consumption accompanied by smoking, exposure to carcinogens such as food preservatives, phenols, air pollutants, hazardous radiations such as UV and X-ray radiation, infections such as syphilis, infection with human papilloma virus or Candida albicans and malnutrition.[6,7]

The signs and symptoms of oral squamous cell carcinoma (OSCC) often include presence of a white, red or mixed white and red plaques, an ulcer with prominent, rigid margins, pain, burning sensation or paresthesia at the site and a prominent fungus- or cauliflower-shaped mass, which are detected during clinical oral examination.

The blood groups are determined based on the presence/absence of some specific hereditary antigens on the surface of red blood cells. The A, B and AB antigens may be present on the surface of red blood cells. Accordingly, the blood groups A, B, AB or O are determined.[3] These antigens are the most important human antigens extensively expressed and found in red blood cells, epithelial cells and body fluids.[7-9] In other words, blood group antigens are among the easiest to find and most accessible expressed genes that can be quickly quantified in humans.[9] These antigens may be related to different diseases since people with some specific antigens may be resistant to some and prone to some other conditions.[10-12] However, this association has yet to be definitely confirmed.[10,13] Immunohistochemical analyses have demonstrated loss of expression of A or B antigens in more than 80% of patients with OSCC. Similarly, potentially malignant lesions with epithelial dysplasia have also shown loss of expression of these antigens.[14,15]

Some studies have pointed to the association of blood group antigens with cancers.[11,12] Rios and Bianca[12] reported that the frequency of blood group A was significantly higher in patients with cancer. They also showed that the Lewis antigen was significantly associated with malignancy. Sharma *et al.*[11] found a significant association between breast cancer and blood type A. Also, they reported that the frequency of blood types B and O was equally higher than other blood types in patients with cervical cancer. The blood type B was predominant in patients with oral mucosal cancer. Xu *et al.*[13] found a significant association between blood type A and endometrial carcinoma. According to Jaleel *et al.*,[5] people with blood type A have 1.46 times higher risk of developing oral cancer. However, according to Xie *et al.*,[16] the correlation of blood type and risk of cancer varies depending on the race and ethnicity of patients. But, adequate evidence is still lacking in this respect.[14,15] Considering the gap of information regarding the

association of blood group and OSCC in Iran, this study aimed to assess the ABO blood group distribution in patients with OSCC.

Materials and Method

This descriptive, analytical study evaluated 113 patients complaining of oral lesions presenting to Imam Reza and Sina Hospitals in Tabriz and Dental School of Tabriz University of Medical Sciences from 2011 to 2014, for whom, a definite diagnosis of OSCC was made. The study was approved in the ethics committee of Qazvin University of Medical sciences (code: IR.QUMS.REC.1395.4). Written informed consent was obtained from all patients and they were ensured about the confidentiality of their information.

The inclusion criterion was confirmed diagnosis of OSCC. The exclusion criteria were unwillingness to participate in the study, tobacco use, alcohol consumption and history of chemotherapy or radiotherapy.

The age and sex of patients, location of the lesion and family history of cancer were recorded. The blood type of patients was determined according to their blood card or by blood typing. Our control group included 2000 blood donors with no systemic disease. The blood type of control subjects was also recorded.

Data were analyzed using SPSS version 16 (SPSS Inc., IL, USA) via analytical (chi-square test and t-test) or descriptive (mean and standard deviation) statistics. Level of significance was set at 0.05.

Results

A total of 133 patients with OSCC were evaluated including 94 males (70.7%) and 39 females (29.3%). The mean age of patients was 67.51±14.29 years (range 30 to 70 years). Of all, 32 patients (24.1%) were in the age range of 60 to 70 years.

Figure 1 shows the age distribution of patients.

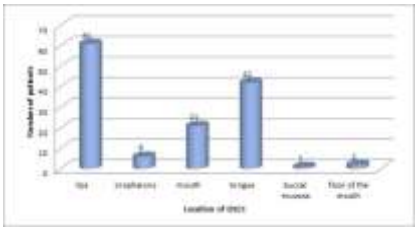

Figure 1: Age distribution of patients

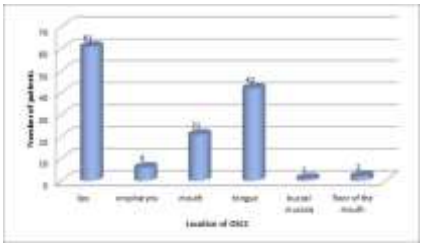

Figure 2: Frequency distribution of patients according to the locations of OSCC

Figure 2 shows the frequency distribution of patients according to the location of OSCC. Lip was the most common site of involvement (n=61, 45.9%).

Regarding the family history of cancer, 23 patients (17.3%) had a positive family history of SCC. Follow-up of patients revealed that 82 patients (61.7%) were cured, 16 (12%) had severe complications, 9 (6.7%) had mild complications and 26 (19.6%) were deceased.

Figure 3 shows the frequency distribution of different blood types. Blood type A (n=45, 33.8%) was the most common blood type.

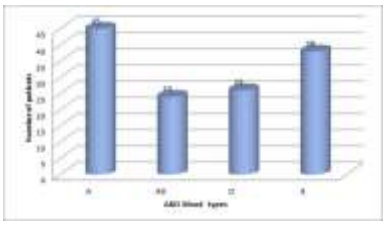

Figure 3: Frequency distribution of different blood types

Comparison of frequency distribution of blood types of controls with patients revealed that the frequency of AB blood type was significantly higher in patients with OSCC while the frequency of O blood type was significantly lower among OSCC patients compared to healthy controls. Table 1 shows the correlation of blood type with occurrence of OSCC. The correlation of occurrence of OSCC with blood type O was evaluated and the results showed that OSCC patients had a significantly lower frequency of this blood type (P=0.001, OR at 95% CI=0.480). The correlation of occurrence of OSCC with blood type A was evaluated and the results showed that OSCC patients had higher a frequency of this blood type but this difference was not statistically significant (P=0.927, OR at 95% CI=1.017). The correlation of occurrence of OSCC with B blood type was evaluated and the results showed that OSCC patients had higher frequency of this blood type but this difference was not statistically significant (P=0.175, OR at 95% CI=1.309).

Blood Type	OSCC Patients		Healthy Patients		p-value
	Frequency	%	Frequency	%	
A	45	33.8	669	33.4	0.000
AB	24	18	191	9.6	
O	26	19.5	672	33.6	
B	38	28.6	468	23.4	

Table 1: Correlation of blood tye with occurence of OSCC

Discussion

This study assessed the ABO blood group distribution in patients with OSCC and showed that blood type A was the most common (33.8%) among OSCC patients. The frequency of blood type AB was significantly higher while the frequency of blood type O was significantly lower in OSCC patients compared to controls. In this study, 133 patients (70.7% males, 29.3% females) with a mean age of

67.51 years were evaluated. Of all patients, 24.1% were in the age range of 60 to 70 years.

The study of Sharma *et al.*[11] was conducted on 82 patients with buccal cancer. Akhtar *et al.*[9] evaluated 560 patients with oral cancer (44% males, 56% females) and 2,640 healthy controls. Gao *et al.*[14] evaluated 24 OSCC patients (70% males and 30% females) with a mean age of 56.29 years. Jaleel *et al.*[6] studied 235 oral cancer patients (32% males, 68% females) that were mostly between 40 to 59 years. They showed that females were significantly more affected than males. Mortazavi *et al.*[1] evaluated 104 patients (66% males, 34% females) and 90 healthy controls. In the patient group, 25% were under 50 years of age while 75% were older than 50 years. Cawson *et al.*[17] reported that oral cancer was age-dependent and 98% of patients in their study were older than 40 years. In the study by Razavi *et al.*,[18] 55% of patients were males and 45% were females with a mean age of 52 years. Our results showed higher frequency of OSCC in males, which was in agreement with the findings of Gao *et al.*,[14] Mortazavi *et al.*,[1] Cawson *et al.*,[17] and Razavi *et al.*[18] This finding may be due to higher frequency of cigarette smoking and tobacco chewing in males and greater exposure to carcinogens in the work environment. Higher frequency of involvement of females in some studies[6,9] may be related to different lifestyle of women such as higher prevalence of cigarette smoking among them or exposure to carcinogens.

In our study, the lips were the most common site of involvement followed by the tongue. In the study by Gao *et al.*[14] tongue was the most common site of involvement (30%) followed by the buccal mucosa (20%). In the study by Jaleel *et al.*[6] buccal mucosa was the most common site of involvement (68%) followed by the tongue (12%), palate (11%) and alveolar bone (12%). Involvement of the lips had the lowest frequency (1%). Razavi *et al.*[18] reported gingival involvement in 46%, tongue involvement in 18%, buccal mucosa involvement in 13%, involvement of the palate in 13% and involvement of the lips in 6%. Variability in the findings of studies regarding the most common site of involvement can be due to different etiologies of OSCC. Higher frequency of lip involvement in our study may suggest the role of sunlight and environmental factors in development of OSCC (instead of carcinogens or chewing tobacco).

ABO and Lewis antigens on the membrane of red blood cells may undergo changes during maturation or malignant transformation (dysplastic changes) of cells. High incidence of some carcinomas has been reported in patients with A/B blood types, which may be due to high affinity of some microorganisms for these antigens, leading to development of malignancies.[15] Several mechanisms have been suggested for the association of ABO blood group and occurrence of malignancies including inflammation, impaired immunity function in finding malignant cells, intracellular adhesion and intracellular signaling.[16] Down-regulation of glycosyltransferase in biosynthesis of A and B antigens can cause an imbalance between the expression of ABO genes and other genes and initiate carcinogenesis.[18,19] ABO antigens also play a role in function of key receptors such as EGF, integrin, cadherin and CD44 and regulate cell proliferation, adhesion and movement. Since the pattern of expression of these receptors widely varies in normal and cancer cells, role of ABO antigens is also widely variable in tumorigenesis.[20] Risk of lip cancer, tongue cancer, gingival cancer, buccal mucosa cancer and carcinoma of the salivary glands is reportedly higher in patients with blood type A.[21] Carcinoma of the salivary glands also occurs in patients with B blood type but with a lower prevalence.[21] Subjects with blood type O are significantly resistant to this type of cancer.[21] Esophageal and laryngeal cancers are more common in patients with blood types A and B but those with blood type O are relatively resistant to esophageal cancer.[21]

In our study, blood type A was the most common (33.8%) among OSCC patients. The results showed that the frequency of blood type AB was significantly higher while the frequency of blood type O was significantly lower in OSCC patients compared to controls. In the study by Sharma *et al.*,[11] the frequency of blood type B was significantly higher among OSCC patients. Biondi *et al.*[20] reported higher prevalence of blood type O among patients with oral cancer. Jaleel *et al.*[6] showed a significant correlation between oral cancer and blood type A ($P<0.05$, OR: 1.46). Mortazavi *et al.*[1] demonstrated that oral cancer patients had significantly lower frequency of blood type O and higher frequency of blood type B compared to the control group. They also compared squamous cell and non-squamous cell cancers and reported higher frequency of blood type B in patients with non-squamous cell cancer. Juvanovic-Cupic *et al.*[22] stated that blood type B was more prevalent in patients with oral and gastrointestinal cancers. Gopal Reddy *et al.*[23] reported that patients with blood group A had higher risk of developing oral submucous fibrosis, which is among the most common premalignant conditions in Indians. Saxena *et al.*[24] evaluated the association of blood group with oral cancer in Western Rajasthan and found that blood group A had the strongest association with oral cancer followed by blood types O and B. Qin *et al.*[25] demonstrated that the overall survival of patients with esophageal, SCC was significantly worse in patients with blood type AB compared to those with other blood groups. This was especially true in patients with negative lymph nodes. A review article by Ramesh *et al.*[26] on studies regarding the association of blood group with oral cancer published between 1965 to 2015 concluded that an inherited element plays a role in susceptibility or resistance to different types of cancers. They added that racial and ethnic distribution of blood groups play a pivotal role in prediction of the risk of cancer.

As shown by our results and those of the afore-mentioned studies, incidence of oral cancer seems to be significantly higher in non-O groups and presence of A and B antigens increases the risk of malignancy. Absence of these antigens (blood type O) decreases this risk. However, sample size, method of sampling, ethnicity and race of patients and

frequency of different blood types in a population all affect the non-O blood type with the greatest association with development of cancer and explains the variability in results in this respect.

Considering the obtained findings, blood typing can be used as a routine method to identify the susceptible individuals and counsel them to minimize the risk factors of OSCC in them as much as possible (i.e. by quitting smoking). Also, regular cancer screening should be scheduled for susceptible individuals. Future studies with larger sample size in different geographical areas are required to better elucidate this topic. Similar studies regarding the relationship of ABO blood group and other types of cancers are also recommended.

Conclusion

The results showed that presence of A and B antigens on cells may increase the risk of OSCC. Blood type O had a significantly lower and blood type AB had a significantly higher frequency among OSCC patients in our study compared to controls.

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